

REMARKS

The Amendments

The amendments to the specification are made to supply serial numbers of U.S. patent applications which were unavailable to the time of filing of the present application, and to correct a filing date of one of the referenced applications. No new matter is introduced by these amendments.

The Sequence Listing

Applicant notes that the Sequence Listing Error Report was prepared by the STIC on June 19, 2000, and points out an error in SEQ ID NO:16. However, on October 30, 2000, a substitute Sequence Listing was mailed to the U.S. Patent and Trademark Office which corrected the error in this sequence. The Error Report which prompted the Notice to Comply therefore predates the substitute Sequence Listing. Applicant therefore believes that no new Sequence Listing is required.

The Examiner has stated that Claims 3 and 4 do not contain a sequence identifier. However, the two sequences cited are actually subsequences of SEQ ID NO:2. The subsequence "SYIVLCIE", which occurs in Claim 3, is a subsequence consisting of amino acid residues 168-175 of SEQ ID NO:2. The amino acid sequence "NSFMTSFSK", which occurs in Claim 4, is a subsequence consisting of amino acid residues 176-184 of SEQ ID NO:2.

Applicant is making a *bona fide* attempt to respond to the Examiner's Communication, but believes that inserting the identifier "SEQ ID NO:2" after these two sequences in the claims would cause the claims to be confusing to the reader, as the same sequence identifier would be referring to what appeared to be two different amino acid sequences.

Because these two subsequences are referred to in the specification (*e.g.*, page 3, lines 26-27), Applicant believes that no separate sequence identifier is necessary for these sequences. In the present case, however, given that there are only two such cited subsequences, Applicant will provide a second substitute Sequence Listing if the Examiner feels that it is necessary, with the two subsequences listed separately in the Sequence Listing, and given their own separate sequence identifiers, separate from SEQ ID NO:2.

The Restriction Requirement

On March 5, 2001, a telephonic Restriction Requirement was received from the Examiner. The Examiner divided the claims into the following eight groups:

- I. Claim 1;
- II. Claims 2-4, 11-16, 35;
- III. Claims 5-10, 32-33;
- IV. Claims 17, 22;
- V. Claims 18-21, 23-25;
- VI. Claims 26-30;
- VII. Claim 31; and
- VIII. Claim 34.

In a subsequent telephone conversation with the Examiner, Attorney Doreen M. Hogle communicated the election of Group II (Claims 2-4, 11-16, and 35) to the Examiner. Because the telephonic election did not provide any opportunity for traversal, Applicant would like to take such opportunity now, and argue for the inclusion of Claim 1 in Group II.

Applicant notes that the necessary criteria for a proper restriction requirement have been clearly defined. Each restriction must meet two separate requirements. These requirements reflect both the statutory basis for restriction under 35 U.S.C. § 121 and its discretionary nature. The criteria are described in the Manual of Patent Examining Procedure (MPEP) at § 803, in relevant part, as follows:

There are two criteria for a proper restriction requirement for restriction between patentably distinct inventions:

- (A) The inventions must be independent . . . or distinct as claimed; and
- (B) There must be a serious burden on the Examiner if restriction is required

Applicant notes that Claim 1 includes as a limitation the amino acid sequence "SYTVLCIE", which is the same subsequence of SEQ ID NO:2 which is included in Claim 3. Applicant therefore believes that a search on the subject matter of Claim 3 will also necessarily produce results relevant to the subject matter of Claim 1. Applicant therefore believes that the subject matter of Claims 1 and 3 is neither independent nor distinct, and that there would be no serious burden on the Examiner if Claim 1 were rejoined with the Claims of Group II. Applicant

therefore respectfully requests that the Restriction Requirement be modified, by rejoining Claim 1 into the Claims of Group II.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (781) 861-6240.

Respectfully submitted,

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.

By


Joyce C. Hersh

Registration No. 42,890

Telephone (781) 861-6240

Facsimile (781) 861-9540

Lexington, Massachusetts 02421-4799

Dated:

June 21, 2001



MARKED UP VERSION OF AMENDMENTS

RECEIVED
JUN 27 2001
RECEIVED

JUN 27 2001

TECH CENTER 1600/2900

Specification Amendments Under 37 C.F.R. § 1.121(b)(1)(iii)

Replace the paragraph at page 17, lines 1 through 10 with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

filed November 16, 1998, and in U.S.S.N. PCT/US98/26058, "Restin and Methods of Use Thereof," by Vikas P. Sukhatme, filed December 8, 1998, and in its U.S. designation U.S.S.N. 09/589,774 [XX/XXX,XXX] and PCT/US98/25892, "Methods of Producing Anti-Angiogenic Proteins," by Vikas P. Sukhatme, filed December 7[8], 1998, and in its U.S. designation U.S.S.N. 09/589,483 [XX/XXX,XXX] the entire teachings of all of which are herein incorporated by reference. Such methods are also included in Dhanabal *et al.* (1999) ("Endostatin Induces Endothelial Cell Apoptosis," *J. Biol. Chem.*, 274:11721-6), and in Dhanabal *et al.* (1999) ("Cloning, Expression and *in vitro* Activity of Human Endostatin," *Bioch. Biophys. Res. Commun.* 258:345-52). Evaluating the ED₅₀ of a mutant in one of the assays described herein is a useful method of comparing activities.

Replace the paragraph at page 15, lines 1 through 8 with the below paragraph marked up by way of bracketing and underlining to show the changes relative to the previous version of the paragraph.

Exemplary methods of producing anti-angiogenic proteins in general, and EM 1 in particular, are provided in the Examples below, and also in PCT/US98/25892, "Methods of Producing Anti-Angiogenic Proteins," by Vikas P. Sukhatme, filed December 7[8], 1998, and its U.S. designation U.S.S.N. 09/589,483, [XX/XXX,XXX,] the entire teachings of which are herein incorporated by reference. The EM 1 protein may also be expressed as a product of transgenic animals, *e.g.*, as a component of the milk of transgenic cows, goats, sheep or pigs, or as a product of a transgenic plant, *e.g.*, combined or linked with starch molecules in maize.